International Journal of Psychophysiology 112 (2017) 46–51

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Aberrant default mode network homogeneity in patients with first-episode treatment-naive melancholic depression

Xilong Cui [a], Wenbin Guo [a], Yi Wang [b], Tian-xiao Yang [b], Xin-hua Yang [c], Yefei Wang [d], Jingbo Gong [d], Changlian Tan [a], Guangrong Xie [a,*]

[a] Mental Health Institute of The Second Xiangya Hospital, Key Laboratory of Psychiatry and Mental Health of Hunan Province, Central South University, Changsha, Hunan 410011, China
[b] Neuropsychology and Applied Cognitive Neuroscience Laboratory, Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China
[c] Institute of Education, Hunan Agricultural University, Changsha, Hunan, China
[d] Department of Applied Psychology, Hunan University of Chinese Medicine, Changsha, Hunan, China

ARTICLE INFO

Article history:
Received 23 April 2016
Received in revised form 2 December 2016
Accepted 14 December 2016
Available online 15 December 2016

Keywords:
Melancholic major depressive disorder
Default mode network
Network homogeneity
Resting-state imaging

ABSTRACT

Background: Melancholic depression is a relatively homogenous subtype of major depressive disorders (MDD). The condition has several endogenous symptoms and represents strong biological components. However, its specific neurobiological mechanisms remain unknown. Previous neuroimaging findings indicated that default mode network (DMN) is closely related to MDD. The present study examined the network homogeneity (NH) of the DMN in patients with melancholic MDD.

Methods: A total of 33 first-episode, treatment-naive melancholic MDD patients and 32 healthy controls underwent a resting-state functional magnetic resonance imaging scan. The data were analyzed using the NH method.

Results: Compared with healthy controls, patients with melancholic MDD showed low NH values in the right middle temporal gyrus and temporal pole (MTG/TP). The abnormal NH of this region and clinical characteristics were not correlated.

Conclusion: Abnormal NH pattern of DMN exists in patients with melancholic MDD. This feature may be part of the pathophysiological basis of this disorder.

1. Introduction

Major depressive disorder (MDD) is one of the most common psychiatric disorders worldwide; the 12-month prevalence of MDD in the United States is 6.7% (Kessler et al., 2005). In 2010, MDD was identified as the second leading cause of disability and the leading cause of burden worldwide (Ferrari et al., 2013). Melancholic MDD, previously described as endogenous or typical depression, is among the most serious subtypes of MDD; this condition has distinctive clinical presentations, such as an abnormal emotional state of unresponsive mood and pervasive anhedonia, psychomotor disturbances, diurnal variation, early morning awakening, excessive guilt, and anorexia (Klein, 1974; Leventhal and Rehm, 2005; Parker et al., 2010). Furthermore, hypercortisolemia, characteristic alterations in sleep architecture, and a superior response to physical treatments compared with psychotherapies have been considered biological indicators of melancholia (Armitage, 2007; Bolwig and Madsen, 2007; Parker et al., 2013, 2010). However, the neurobiological underpinnings of melancholic MDD remain unknown.

Recent three-dimensional structural magnetic resonance imaging (MRI) studies showed that patients with melancholic MDD demonstrated increased cerebrospinal fluid space (CSF) volume surrounding the Sylvian fissure (Cardoner et al., 2003; Pujol et al., 2002; Via et al., 2012), particularly in the left hemisphere (Cardoner et al., 2003; Pujol et al., 2002). CSF volume reduction was also observed in the subarachnoid spaces around the medial and lateral parietal cortices (Via et al., 2012). Decreased gray matter (GM) volume in the left insula and increased white matter (WM) volume in the upper brainstem tegmentum were reported in melancholic patients (Soriano-Mas et al., 2011). Diffusion tensor imaging study showed that melancholic MDD is associated with the alteration of WM microstructure in the medial forebrain bundle (Bracht et al., 2014). Moreover, only a few functional neuroimaging

Abbreviations: MDD, major depressive disorder; DMN, default mode network; NH, network homogeneity; MRI, magnetic resonance imaging; GM, gray matter; CSF, cerebrospinal fluid space; WM, white matter; ACC, anterior cingulate cortex; MPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; PCu, precuneus; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; HRSD-17, 17-item Hamilton Rating Scale for Depression; IQ, intelligence quotient; SHAPS-C, Chinese version of Snaith–Hamilton Pleasure Scale; EPI, echo planar imaging; DARTEL, diffeomorphic anatomical registration through exponentiated lie algebra method; FWHM, full-width at half-maximum; ROI, seed-based region of interest; FC, functional connectivity; ICA, independent component analysis; MTG, middle temporal gyrus; TP, temporal pole.

* Corresponding author at: Building 139, Renmin Middle Road, Changsha 410011, China.
E-mail address: xiegrpsy@126.com (G. Xie).

http://dx.doi.org/10.1016/j.ijpsycho.2016.12.005
0167-8760/

studies on melancholic MDD have been conducted. Melancholic MDD patients showed disengagement of the ventromedial prefrontal cortex and significantly higher neuronal activities of subgenual anterior cingulate cortex (ACC) in task-related studies (Baeken et al., 2010; Guo et al., 2015). Findings from a rare resting-state study showed reduced effective connectivity between insular and executive networks in melancholic MDD patients (Hyett et al., 2015). To date, only a few researchers have conducted resting-state studies on melancholic MDD by focusing on the default mode network (DMN), which has been reported to play a vital role in the pathophysiology of MDD (Broyd et al., 2009; Silbersweig, 2013).

The DMN refers to a group of brain regions which are mostly active in the resting state, namely, the medial prefrontal cortex (MPFC), ventral ACC, posterior cingulate cortex (PCC), precuneus (PCu), inferior parietal lobule, lateral parietal cortex, medial parietal cortex, and extended lateral temporal gyrus (Fox and Raichle, 2007; Raichle et al., 2001; Sheline et al., 2009). Previous studies have speculated that the DMN is involved in spontaneous thinking production (Mason et al., 2007), self-consciousness maintenance (Gusnard et al., 2001), and self-related processes, including memory, cognition, and emotion (Buckner and Carroll, 2007; Cabeza et al., 2002; Lemogne et al., 2010). Moreover, the self-related processes provide an intuitive basis of rumination in MDD (Hamilton et al., 2015). Numerous studies showed abnormal DMN alteration in patients with MDD (Alexopoulos et al., 2012; Chen et al., 2015; Korgaonkar et al., 2014; Zhu et al., 2012), including our previous study (Guo et al., 2014b; Liu et al., 2012a), but the results are inconsistent. Aside from different methods and the influence of medications, the heterogeneity of different MDD subtypes may contribute to the inconsistent outcomes, suggesting that further investigations should focus on homogenous subgroups.

In the present study, we detected the network homogeneity (NH) (Uddin et al., 2008) of DMN in patients with melancholic MDD to probe the neurobiological signature of this refined depression subtype. We hypothesized that melancholic MDD patients would exhibit an abnormal NH pattern of DMN. The second objective of the study was to explore the association between the abnormal NH and the clinical variables of this disorder, particularly the anhedonia severity.

2. Materials and methods

2.1. Participants

We recruited 33 first-episode, treatment-naive melancholic MDD outpatients from the Second Xiangya Hospital, Central South University, China. The diagnosis was independently ascertained by two psychiatrists, according to the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (*DSM-IV*) criteria (American Psychiatric Association, 1994). All patients met the criteria for MDD with melancholic features, which required (1) pervasive anhedonia and/or nonreactive mood and (2) three (or more) of the following: characteristic depressive mood, regularly worse in the morning, early morning awakening, marked psychomotor agitation or retardation, significant anorexia or weight loss, and excessive or inappropriate guilt. The 17-item Hamilton Rating Scale for Depression (HRSD-17) (Hamilton, 1967) was administered to assess depression severity in patients with melancholic MDD. Patients were only eligible for the study if they were in a current major depressive episode with a HRSD-17 total score of ≥17 on the day of the MRI examination, with an illness duration of <12 months. All patients had no history of psychotic drug and electroconvulsive therapy. The exclusion criteria were: (1) past or present Axis I or Axis II diagnosis (except in MDD patients) as assessed by the Structured Clinical Interview for *DSM-IV* (First et al., 1997); (2) history of neurological disorders, severe physical illnesses, and substance abuse; (3) pregnancy; (4) an estimated intelligence quotient (IQ) below 80 as tested by the Chinese version of the revised Wechsler Adult Intelligence Scale (Gong, 1992); (5) abnormal cerebral structure after initial MRI scanning.

A total of 32 age-, gender-, and education-matched healthy controls were recruited from the community with the same exclusion criteria for the patients with melancholic MDD. All subjects were right-handed. None of the controls had a family history of neuropsychiatric illness or severe medical condition in their first-degree relatives. The Chinese version of Snaith-Hamilton Pleasure Scale (SHAPS-C) (Liu et al., 2012b) was administered to all the patients and controls to assess anhedonic states.

The study was approved by the Medical Research Ethics Committee of the Second Xiangya Hospital, Central South University, China. Informed consent was obtained from all subjects before enrollment.

2.2. Image acquisition

MRI data was acquired with a Siemens 3.0 T scanner. T1-weighted volumetric 3D images were obtained by a spoiled gradient recall sequence with the following parameters: repetition time = 2000 ms; echo time = 2.26 ms; inversion time = 900 ms; flip angle = 8°; acquisition matrix = 256 × 256; field of view = 256 × 240 mm^3; slice thickness = 1 mm; no slice gap; number of slices = 176. All participants underwent the resting-state scan by the echo planar imaging (EPI) sequence with the following parameters: repetition time/echo time = 2500/25 ms; 39 slices; matrix = 64 × 64; flip angle = 90°; field of view = 240 mm × 240 mm; slice thickness = 3.5 mm; no gap; number of volumes = 200. The participants were instructed to lay supine, remain motionless, keep their eyes closed, and stay awake during the scan.

2.3. Data preprocessing

The structural images were preprocessed with the VBM toolbox (VBM8, http://dbm.neuro.uni-jena.de/vbm) of the Statistical Parametric Mapping software package (SPM8, http://www.fil.ion.ucl.ac.uk/spm). Structural images were segmented to GM, WM, and CSF. High-dimensional normalization by the diffeomorphic anatomical registration through exponentiated lie algebra method (DARTEL) (Ashburner, 2007) was used to register the segmented images to the Montreal Neurological Institute (MNI) space. Tissue deformation was applied to modulate the segmented GM images. Finally, the normalized and modulated volumes (voxel size, 1.5 × 1.5 × 1.5 mm^3) were smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian kernel.

Functional data preprocessing was conducted in MATLAB (MathWorks) with the data processing assistant for resting-state fMRI (DPARSF) (Chao-Gan and Yu-Feng, 2010). After slice timing and head motion correction, the data of two patients were excluded because of excessive head motion (≥2° of maximal rotation or ≥2 mm of maximal translation). We also removed the spurious covariates, such as the signal from the WM-centered region and the ventricular seed-based region of interest (ROI), and the 24-head motion parameters, which were obtained by rigid body correction. As previously suggested, the global signal was preserved while preprocessing the functional connectivity (FC) data (Hahamy et al., 2014). We reoriented and co-registered the T1 images to the mean functional images. A unified segmentation algorithm segmented the T1 images into GM, WM, and CSF (Ashburner and Friston, 2005; Kybic et al., 2000; Nichols et al., 2016). The functional images were spatially normalized to the MNI space and resampled to 3 mm × 3 mm × 3 mm voxels with the normalization parameters, which were estimated during unified segmentation. The normalized and modulated volumes were smoothed with an 8 mm FWHM Gaussian kernel. Finally, the functional voxels were temporally band-pass filtered (0.01–0.08 Hz) and linearly detrended.